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The Two-Sided Face of Antidepressants: The Impact of Their Use on Real-Life Affective Change during Mindfulness-Based Cognitive Therapy

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Antidepressant medication (AD) is the most often used treatment for major depressive disorder (MDD), prescribed to an estimated 73.8% of the MDD patients in care in 2007 [1]. However, many patients with MDD who experience full symptomatic remission after AD treatment still have residual depressive symptoms, which have been associated with continued impaired functioning [2]. The sequential addition of psychotherapy to pharmacotherapy has therefore been considered, and shown, to offer a better possibility of improving long-term outcome in terms of reduced relapse/recurrence [3]. Since positive emotions play a crucial role in the development of long-term personal skills and resources through broadening awareness and behavioural repertoires [4], it is of interest to examine whether adding psychotherapy to AD treatment has beneficial effects on positive emotional experiences.

We explored this question in a randomized controlled trial of mindfulness-based cognitive therapy (MBCT) versus a waiting list control group (WLCG), based upon which it was previously shown that MBCT increases positive affect (PA) in people with residual depressive symptoms [5]. Participants in this randomized controlled trial were asked to continue any pharmacological treatment during participation in the study, hence providing us with a subgroup of people taking ADs. It was investigated whether this subgroup responded differently to MBCT treatment in terms of both PA and negative affect (NA).

Neuroimaging research has shown that ADs can diminish the neural processing of both rewarding and aversive stimuli in healthy controls when investigating the placebo-controlled effect [6]. This could account for the experience of emotional blunting described by some patients during selective serotonin reuptake inhibitor treatment [7]. Hence it seems that some ADs can suppress the brain system that is important for the generation of positive emotions (reward system) in addition to the one generating negative emotions (stress system). It was therefore hypothesized that AD and MBCT have a synergistic effect on NA but that AD inhibits the positive effect of MBCT on PA.

In the trial, individuals (n = 129) with residual depressive symptoms (score ≥7 on the 17-item Hamilton Depression Rating Scale after at least 1 prior episode of MDD) were randomized to either MBCT or WLCG [for details on the procedures, see 4]. One of the exclusion criteria for participation was recent (in the past 4 weeks) or upcoming changes in ongoing psychological or pharmacological treatment. PA (mean of items: I feel 'happy', 'satisfied', 'strong', enthusiastic', 'curious', cheerful' and 'inspired') and NA (mean of items: I feel 'down', 'anxious', 'lonely', 'suspicious', 'disappointed', 'insecure' and 'guilty') were assessed using experience sampling methodology before and after the treatment (or waiting list) period. Analyses were executed with the XTMIXED command when they concerned multilevel data and LOGIT and REGRESS commands for, respectively, dichotomous and quantitative unilevel data in STATA 12.1.

Since AD use was not randomized within treatment groups, potential confounder variables were examined. It was investigated whether (a) treatment groups (MBCT and WLCG) differed in their AD use, and (b) participants taking ADs (AD+) differed from participants not taking ADs (AD–) with regard to the outcome measures at baseline (PA, NA) or potential confounding variables (table 1) both overall as well as within treatment groups (MBCT and WLCG). Based on these analyses only antipsychotic use was found to be a potential confounder.

Significant three-way interaction [MBCT/WLCG × time (pre/post) × AD (yes/no)] effects were found for both NA ($b = -0.208$, $p = 0.001$) and PA ($b = -0.171$, $p = 0.031$) and these effects remained significant after controlling for the interaction of antipsychotic use with time and group (NA: $b = -0.207$, $p = 0.002$; PA: $b = -0.187$, $p = 0.023$).

NA: When stratifying the analysis by use of ADs (i.e., two-way interaction: MBCT/WLCG × time), the impact of MBCT (compared to WLCG) on decrease in NA was stronger in AD+ ($b = -0.424$, $p < 0.001$) than in AD– ($b = -0.216$, $p < 0.001$). The results of the three-way interaction analysis (see above) indicated that this difference was statistically significant. PA: When stratifying the

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Table 1. Characteristics of treatment group combinations

	MBCT		WLCG	
	AD–	AD+	AD–	AD+
Patients, n	42	21	41	25
NA (baseline)	2.0±1.1	2.1±1.1	2.1±1.1	1.9±1.0
PA (baseline)	3.6±1.3	3.6±1.3	3.7±1.2	3.9±1.2
Male gender, %	24	14	32	20
Age, years	44.3±9.8	44.5±9.8	41.9±9.9	45.4±8.6
Previous depressive episodes (3 or more), %	40	55	39	52
YTQ total score	43.8±13.7	45.8±15.3	46.3±17.1	43.6±15.3
HDRS total score at baseline	10.6±3.7	10.0±3.2	10.4±3.3	9.9±4.0
Total minutes practiced during MBCT	1,526±621	1,310±699		
Taking anxiolytic medication, %	17	24	10	20
Taking antipsychotic medication, %	0	19	2	4
Psychotherapy, %	19	29	18	8
Counselling, %	7	24	5	24
SSRI, n		14		20
TCA, n		4		0
SNRI, n		1		0
MAOI, n		0		1
SARI, n		1		1
NaSSA, n		0		2
NaSSA and SDRI, n		1		0
SARI and SNRI, n		0		1

Values represent number, mean ± SD or percentage. YTQ = Youth Trauma Questionnaire; HDRS = Hamilton Depression Rating Scale; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; SNRI = serotonin and norepinephrine reuptake inhibitor; MAOI = monoamine oxidase inhibitor; SARI = serotonin antagonist and reuptake inhibitor; NaSSA = noradrenergic and specific serotonergic antidepressant; SDRI = serotonin-dopamine reuptake inhibitor.

analysis by use of ADs, the impact of MBCT (compared to WLCG) on increase in PA was stronger in AD– ($b = 0.543$, $p < 0.001$) than in AD+ ($b = 0.372$, $p < 0.001$). The results of the three-way interaction analysis (see above) indicated that this difference was statistically significant.

The hypothesis concerning NA was therefore confirmed: MBCT with subjects taking AD ($MBCT_{AD+}$) decreases NA more than only AD in combination with WLCG ($WLCG_{AD+}$), indicating a beneficial effect of sequentially adding psychotherapy to AD. Additionally, the $MBCT_{AD+}$ group showed a larger decrease in NA compared to people receiving MBCT while not taking AD ($MBCT_{AD-}$). Hence it appears that AD and MBCT treatment have a synergistic effect in decreasing daily life negative emotions.

With regard to PA the hypothesis was additionally confirmed. Adding MBCT to AD ($MBCT_{AD+}$) increased PA more than just AD in combination with WLCG ($WLCG_{AD+}$), again indicating a beneficial effect of sequentially adding psychotherapy to AD. However, the $MBCT_{AD+}$ group showed a *smaller* increase in PA compared to people receiving MBCT while *not* receiving AD ($MBCT_{AD-}$). These results are in line with the neuroimaging research showing that ADs seem to dampen the brain reward system responsible for the experience of these emotions [6].

In summary, sequentially adding psychotherapy to AD in the treatment of residual depressive symptoms seems beneficial in that it both decreases NA and increases PA. However, in terms of PA, the group that showed the largest increase were the participants *without* AD who received MBCT treatment. Since the generation of positive emotions is crucial in the initiation of a positive spiral towards recovery [4], long-term outcomes of this contingent inhibiting effect of AD on psychotherapy outcome in terms of PA will have to be investigated in more detail in experimental set-ups. If our findings are replicated it would implicate that the sequential addition of psychotherapy to AD could be less efficient than discontinuing AD before/during receiving psychotherapy especially for improving long-term outcomes.

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Disclosure Statement

The authors declare no conflict of interest.

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